Supplementary Appendix to:

Effectiveness of a bivalent mRNA vaccine dose against symptomatic SARS-CoV-2 infection among U.S. healthcare personnel, September 2022–May 2023

Supplementary Table 1: Types of healthcare facility included in the study of bivalent mRNA COVID-19 vaccine effectiveness among U.S. healthcare personnel

Facility Type	# (%)
Acute care hospital	62 (48.4)
Home health	2 (1.5)
Outpatient	27 (21.1)
Rehabilitation	2 (1.5)
Emergency department	4 (3.1)
SNF/Nursing home/Long-term care	8 (6.3)
Urgent care center	22 (17.2)
FHC/Community health center	1 (0.8)
Total	**128**

SNF: skilled nursing facility; FHC: family health center

Supplementary Box 1: Occupational groups included in the definition of healthcare personnel in the study

- Administrative staff
- Chaplain
- Cytotechnologist
- Environmental services worker
- Facilities/maintenance worker
- Food services worker
- Histotechnologist
- Home health aide/caregiver
- Laboratory personnel
- Licensed practical nurse
- Medical assistant
- Medical laboratory technician
- Medical/clinical lab scientist
- Nurse practitioner
- Nursing assistant
- Nutritionist
- Occupational therapist
- Other laboratory personnel
- Pharmacist or pharmacy personnel
- PhD laboratory scientist
- Phlebotomist
- Physical therapist
- Physician (attending)
- Physician (fellow)
- Physician (intern/resident)
- Physician assistant
- Registered nurse
- Respiratory therapist
- Social worker
- Speech therapist
- Student
- Ward clerk

Supplementary Box 2: COVID-19–like symptoms defined for analysis purposes

- Abdominal pain
- Altered sense of smell or taste
- Chest pain/tightness
- Chills
- Congestion
- Diarrhea
- Documented fever ≥100.0°F
- Dry cough
- Fatigue or malaise
- Felt feverish
- Headache
- Loss of appetite
- Muscle aches
- Nausea or vomiting
- Productive cough
- Red or bruised toes or feet
- Runny nose
- Shortness of breath
- Sore throat

Supplementary Table 2: Categorization of underlying health conditions among U.S. healthcare personnel

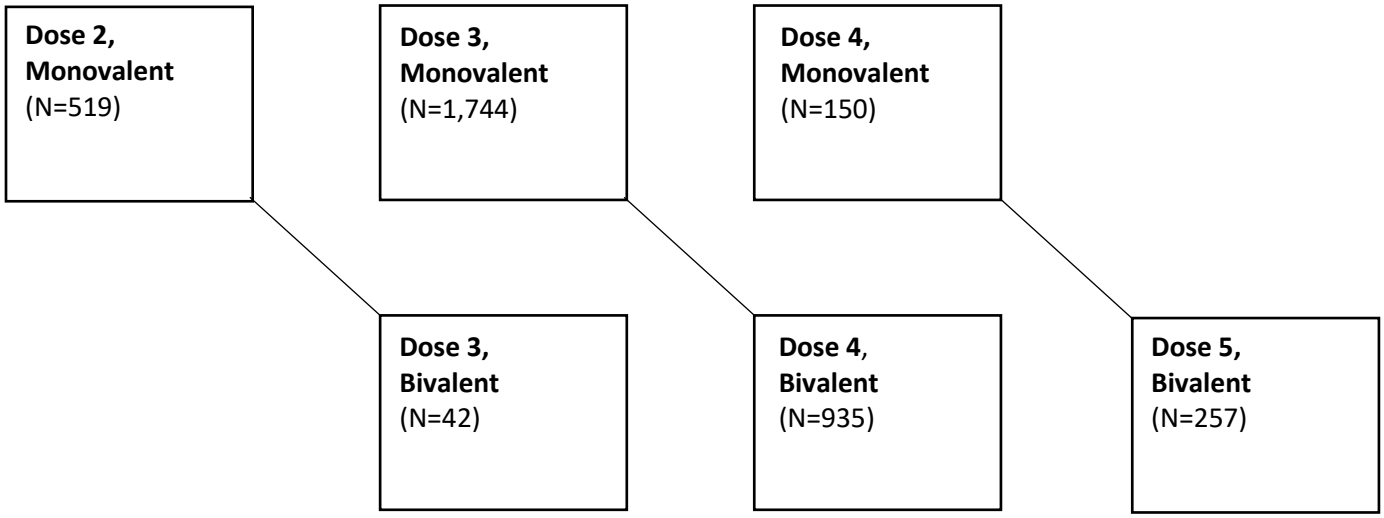
Category	Notes	Source from survey	Source from medical chart
Pulmonary disease	Includes asthma, chronic pulmonary disease	Questions on asthma, COPD, other pulmonary disease; free text	Questions on asthma, COPD, other pulmonary disease; free text
Cardiac disease	Cardiac disease, excluding hypertension, peripheral vascular disease, or findings that might not be pathologic	Question on cardiovascular disease; free text	Question on cardiovascular disease; free text
Liver disease	Chronic liver disease	Question on chronic liver disease; free text	Question on chronic liver disease; free text
Renal disease	Chronic renal disease, including renal dialysis patients	Questions on chronic renal disease, renal dialysis; free text	Questions on chronic renal disease, renal dialysis; free text
Diabetes mellitus type 1 or 2	Excludes pre-diabetes	Question on diabetes; free text	Question on diabetes, free text
Obesity	Based on clinical diagnosis or BMI	Reported BMI ≥30	Question on obesity, BMI ≥30
Overweight without obesity	Excludes diagnosis of obesity	Reported BMI ≥25 and BMI<30	BMI ≥25 and BMI<30
Cancer	Current or previous solid organ or hematologic cancer	Question on history of cancer; free text	Question on history of cancer; free text
Immunocompromised	Includes list of any specific condition or medication associated with immunocompromised state, including HIV, hematopoietic stem cell or solid organ transplant	Question on survey regarding medication or conditions, or free text, *if* specific medications or conditions listed that are associated with immunocompromise	Questions on any specific condition or medication associated with immunocompromised state, including HIV, hematopoietic stem cell or solid organ transplant
Mood disorder	Limited to depressive and mood disorders, including schizophrenia	Free text	Free text
Smoking or substance abuse	Current or previous cigarette smoking	Question on history of smoking; free text	Question on history of smoking; free text
Other diagnosis	Other conditions contributing to the definition of 'underlying health condition': congenital disorders, neurodegenerative disorders, sickle cell disease or thalassemia major, TB disease.	Free text	Free text
Pregnancy	Current pregnancy on date of survey	Question on pregnancy and gestation	Question on pregnancy and gestation

Abbreviation: BMI – body mass index in kg/m^2

Supplementary Table 3: States of participating health facilities for case- and control-participants included in the analysis of bivalent mRNA VE against COVID-19 among U.S. healthcare personnel

State	No. Case-participants	No. Control-participants	Total
Alabama	30 (2.0%)	15 (0.7%)	45 (1.2%)
Arizona	24 (1.6%)	13 (0.6%)	37 (1.0%)
California	98 (6.4%)	175 (8.3%)	273 (7.5%)
Colorado	47 (3.1%)	93 (4.4%)	140 (3.8%)
Connecticut	37 (2.4%)	34 (1.6%)	71 (1.9%)
Florida	19 (1.2%)	8 (0.4%)	27 (0.7%)
Georgia	30 (2.0%)	23 (1.1%)	53 (1.5%)
Iowa	36 (2.4%)	15 (0.7%)	51 (1.4%)
Illinois	53 (3.5%)	159 (7.5%)	212 (5.8%)
Louisiana	27 (1.8%)	11 (0.5%)	38 (1.0%)
Massachusetts	262 (17.2%)	430 (20.3%)	692 (19.0%)
Maryland	20 (1.3%)	41 (1.9%)	61 (1.7%)
Missouri	134 (8.8%)	160 (7.6%)	294 (8.1%)
Mississippi	3 (0.2%)	0 (0%)	3 (0.1%)
North Carolina	44 (2.9%)	145 (6.8%)	189 (5.2%)
New Mexico	5 (0.3%)	4 (0.2%)	9 (0.2%)
New York	277 (18.1%)	665 (31.4%)	942 (25.8%)
Oregon	86 (5.6%)	49 (2.3%)	135 (3.7%)
Pennsylvania	273 (17.9%)	27 (1.3%)	300 (8.2%)
Tennessee	8 (0.5%)	42 (2.0%)	50 (1.4%)
Utah	14 (0.9%)	9 (0.4%)	23 (0.6%)
Washington	1 (0.1%)	1 (0%)	2 (0.1%)
TOTAL	1,528	2,119	3,647

Supplementary Figure 1: Categories of vaccination status used to assess the benefit of a bivalent booster dose



Diagonal lines indicate a comparison between receipt of a monovalent dose only (top row) and a bivalent dose (bottom row) a. Vaccination status was defined on the test date as 'monovalent', if the last dose was a monovalent mRNA vaccine dose 2, 3, or 4 administered ≥67 days previously, or as 'bivalent' if a monovalent dose 2, 3 or 4 was administered ≥67 days previously *and* the last dose was a bivalent mRNA dose 3, 4 or 5 administered ≥7 days previously. Participants who did not meet these definitions or who received a non-mRNA dose were excluded from the analysis.

Supplementary Table 4: Additional Characteristics of Healthcare Personnel with COVID-19 (Case-participants) or who tested negative for SARS-CoV-2 (Control-participants)

Characteristic	Case-participants No. with characteristic / Total (%)	Control-participants No. with characteristic / Total (%)	SMD
In 2-week stratum by site with both case- and control-participants			
No	1409/1528 (92.2%)	2011/2119 (94.9%)	0.110
Yes	119/1528 (7.8%)	108/2119 (5.1%)	0.110
In 4-week stratum by U.S. census region with both case- and control-participants			
No	1528/1528 (100%)	2118/2119 (100%)	0.031
Yes	0/1528 (0%)	1/2119 (0%)	0.031
U.S. census region			
Midwest	223/1528 (14.6%)	334/2119 (15.8%)	0.033
Northeast	849/1528 (55.6%)	1156/2119 (54.6%)	0.020
South	181/1528 (11.8%)	285/2119 (13.4%)	0.048
West	275/1528 (18.0%)	344/2119 (16.2%)	0.047
Health insurance			
Private	1381/1525 (90.6%)	1904/2115 (90.0%)	0.018
Government	72/1525 (4.7%)	102/2115 (4.8%)	0.005
Other	7/1525 (0.5%)	14/2115 (0.7%)	0.027
No insurance	65/1525 (4.3%)	95/2115 (4.5%)	0.011
Annual household income, $			
<50,000	203/1524 (13.3%)	292/2117 (13.8%)	0.014
50,000–100,000	500/1524 (32.8%)	709/2117 (33.5%)	0.014
≥100,000	665/1524 (43.6%)	903/2117 (42.7%)	0.020
Declined	156/1524 (10.2%)	213/2117 (10.1%)	0.006
Work in an emergency department or hospital?			
No	465/1528 (30.4%)	691/2119 (32.6%)	0.047
Yes	1063/1528 (69.6%)	1428/2119 (67.4%)	0.047
Level of anticipated direct patient contact			
Substantial	495/1528 (32.4%)	642/2119 (30.3%)	0.045
Moderate	110/1528 (7.2%)	175/2119 (8.3%)	0.040
Minimal	902/1528 (59.0%)	1280/2119 (60.4%)	0.028
Undefined	21/1528 (1.4%)	22/2119 (1.0%)	0.031
Exposures representing possible risk in the community			
Close contact with an ill person	460/1420 (32.4%)	717/1918 (37.4%)	0.073
Attended gathering with non-household members	835/1494 (55.9%)	1148/2061 (55.7%)	0.022
Public transport	350/1498 (23.4%)	468/2082 (22.5%)	0.026
Shared transport	281/1496 (18.8%)	456/2088 (21.8%)	0.073
Attended daycare or school	458/1343 (34.1%)	744/1880 (39.6%)	0.108
Household member in daycare	88/1498 (5.9%)	171/2086 (8.2%)	0.089
Hospitalized within 14 days of index test date?			
No	1060/1076 (98.5%)	1481/1526 (97.1%)	0.099
Yes	16/1076 (1.5%)	45/1526 (2.9%)	0.099

Supplementary Table 5: Differences in characteristics of U.S. healthcare personnel by most recent vaccine dose received, September 2022–May 2023

	Monovalent dose 2 (N = 519)	Monovalent dose 3 (N = 1,744)	Bivalent dose 3 (N = 42)	Monovalent dose 4 (N = 150)	Bivalent dose 4 (N = 935)	Bivalent dose 5 (N = 257)
Age group, years						
18–29	155/519 (29.9%)	441/1744 (25.3%)	14/42 (33.3%)	7/150 (4.7%)	180/935 (19.3%)	11/257 (4.3%)
30–39	184/519 (35.5%)	611/1744 (35.0%)	15/42 (35.7%)	21/150 (14.0%)	372/935 (39.8%)	17/257 (6.6%)
40–49	97/519 (18.7%)	356/1744 (20.4%)	7/42 (16.7%)	16/150 (10.7%)	211/935 (22.6%)	17/257 (6.6%)
≥50	83/519 (16.0%)	336/1744 (19.3%)	6/42 (14.3%)	106/150 (70.7%)	172/935 (18.4%)	212/257 (82.5%)
Sex						
Male	66/519 (12.7%)	271/1744 (15.5%)	9/42 (21.4%)	29/150 (19.3%)	191/935 (20.4%)	58/257 (22.6%)
Female	453/519 (87.3%)	1473/1744 (84.5%)	33/42 (78.6%)	121/150 (80.7%)	744/935 (79.6%)	199/257 (77.4%)
Race and ethnicity						
White, non-Hispanic	300/519 (57.8%)	1251/1744 (71.7%)	22/42 (52.4%)	117/150 (78.0%)	741/935 (79.3%)	227/257 (88.3%)
Black, non-Hispanic	101/519 (19.5%)	162/1744 (9.3%)	7/42 (16.7%)	13/150 (8.7%)	51/935 (5.5%)	8/257 (3.1%)
Hispanic	93/519 (17.9%)	195/1744 (11.2%)	10/42 (23.8%)	9/150 (6.0%)	59/935 (6.3%)	10/257 (3.9%)
Other, non-Hispanic	25/519 (4.8%)	136/1744 (7.8%)	3/42 (7.1%)	11/150 (7.3%)	84/935 (9.0%)	12/257 (4.7%)
Highest educational level						
College degree or less	487/519 (93.8%)	1500/1744 (86.0%)	37/42 (88.1%)	123/150 (82.0%)	674/935 (72.1%)	185/257 (72.0%)
Doctoral or professional degree	32/519 (6.2%)	244/1744 (14.0%)	5/42 (11.9%)	27/150 (18.0%)	261/935 (27.9%)	72/257 (28.0%)
Underlying health conditions[1]						
0	94/519 (18.1%)	416/1744 (23.9%)	4/42 (9.5%)	19/150 (12.7%)	281/935 (30.1%)	44/257 (17.1%)
1	222/519 (42.8%)	774/1744 (44.4%)	26/42 (61.9%)	69/150 (46.0%)	390/935 (41.7%)	100/257 (38.9%)
≥2	203/519 (39.1%)	554/1744 (31.8%)	12/42 (28.6%)	62/150 (41.3%)	264/935 (28.2%)	113/257 (44.0%)
Period of test						
Q3 2022	40/519 (7.7%)	223/1744 (12.8%)	0/42 (0%)	28/150 (18.7%)	11/935 (1.2%)	2/257 (0.8%)
Q4 2022	259/519 (49.9%)	724/1744 (41.5%)	11/42 (26.2%)	71/150 (47.3%)	347/935 (37.1%)	116/257 (45.1%)
Q1 2023	198/519 (38.2%)	680/1744 (39.0%)	26/42 (61.9%)	40/150 (26.7%)	474/935 (50.7%)	110/257 (42.8%)
Q2 2023	22/519 (4.2%)	117/1744 (6.7%)	5/42 (11.9%)	11/150 (7.3%)	103/935 (11.0%)	29/257 (11.3%)
Reason for test						
Symptoms	424/499 (85.0%)	1427/1706 (83.6%)	31/38 (81.6%)	106/145 (73.1%)	735/911 (80.7%)	182/244 (74.6%)

[1] Number of underlying conditions, using categories defined in Supplementary Table 2.

	Monovalent dose 2 (N = 519)	Monovalent dose 3 (N = 1,744)	Bivalent dose 3 (N = 42)	Monovalent dose 4 (N = 150)	Bivalent dose 4 (N = 935)	Bivalent dose 5 (N = 257)
Exposure, no symptoms	35/499 (7.0%)	129/1706 (7.6%)	2/38 (5.3%)	13/145 (9%)	83/911 (9.1%)	23/244 (9.4%)
Other	40/499 (8.0%)	150/1706 (8.8%)	5/38 (13.2%)	26/145 (17.9%)	93/911 (10.2%)	39/244 (16.0%)
Known prior infection[2]						
No	224/519 (43.2%)	980/1744 (56.2%)	18/42 (42.9%)	109/150 (72.7%)	546/935 (58.4%)	206/257 (80.2%)
Yes, >12 months ago, or before Omicron predominance	159/519 (30.6%)	307/1744 (17.6%)	9/42 (21.4%)	15/150 (10.0%)	128/935 (13.7%)	14/257 (5.4%)
Yes, within 12 months and after Omicron predominance	136/519 (26.2%)	457/1744 (26.2%)	15/42 (35.7%)	26/150 (17.3%)	261/935 (27.9%)	37/257 (14.4%)
Days since last monovalent dose						
0-	3/519 (0.6%)	1/1744 (0.1%)	0/42 (0%)	8/150 (5.3%)	0/935 (0%)	1/257 (0.4%)
90-	5/519 (1.0%)	16/1744 (0.9%)	0/42 (0%)	73/150 (48.7%)	1/935 (0.1%)	35/257 (13.6%)
180-	13/519 (2.5%)	126/1744 (7.2%)	1/42 (2.4%)	50/150 (33.3%)	11/935 (1.2%)	128/257 (49.8%)
270-	40/519 (7.7%)	544/1744 (31.2%)	1/42 (2.4%)	14/150 (9.3%)	70/935 (7.5%)	77/257 (30.0%)
360-	68/519 (13.1%)	704/1744 (40.4%)	7/42 (16.7%)	3/150 (2.0%)	404/935 (43.2%)	14/257 (5.4%)
450-	390/519 (75.1%)	353/1744 (20.2%)	33/42 (78.6%)	2/150 (1.3%)	449/935 (48.0%)	2/257 (0.8%)
Days since last dose						
0-	3/519 (0.6%)	1/1744 (0.1%)	23/42 (54.8%)	8/150 (5.3%)	429/935 (45.9%)	130/257 (50.6%)
90-	516/519 (99.4%)	1743/1744 (99.9%)	19/42 (45.2%)	142/150 (94.7%)	506/935 (54.1%)	127/257 (49.4%)
Dose timing (Median, range)						
Days between dose and previous dose	22 (14, 527)	283 (64, 554)	559 (152, 679)	225 (94, 334)	348 (103, 490)	155 (68, 358)
Days since last dose	578 (67, 821)	382 (68, 604)	80 (11, 224)	172 (72, 509)	95 (7, 256)	89 (7, 247)
Days since last monovalent dose	578 (67, 821)	382 (68, 604)	635 (247, 843)	172 (72, 509)	447 (161, 602)	244 (81, 492)

[2] Prior infection defined as self-reported positive SARS-COV-2 nucleic acid amplification test or antigen test result >90 days before test date; Omicron predominance defined based on national estimates as on or after 12/19/2021.

Supplementary Table 6: Estimated Vaccine Effectiveness of a bivalent mRNA dose against symptomatic SARS-CoV-2 infection among U.S. healthcare personnel (using unadjusted models)

Characteristic	No. case-participants who received a bivalent dose / No. eligible (%)[3]	No. control-participants who received a bivalent dose / No. eligible (%)	Unadjusted vaccine effectiveness (95% CI)[4]
Bivalent product			
Any mRNA	443/1528 (29.0%)	791/2119 (37.3%)	**26.2 (14.4-36.3)**
Pfizer BioNTech	337/1422 (23.7%)	593/1921 (30.9%)	**25.2 (11.8-36.5)**
Moderna	106/1191 (8.9%)	198/1526 (13.0%)	**28.4 (7.5-44.6)**
Days since bivalent dose			
7–59	112/1197 (9.4%)	228/1556 (14.7%)	**50.7 (36.5-61.8)**
≥60	331/1416 (23.4%)	563/1891 (29.8%)	**11.7 (-4.8-25.7)**
Days since last monovalent dose			
67-359	125/572 (21.9%)	200/646 (31.0%)	**32.6 (11.4-48.7)**
≥360	318/956 (33.3%)	591/1473 (40.1%)	**23.7 (9.3-35.9)**
Number of monovalent doses			
Two	14/258 (5.4%)	28/303 (9.2%)	**41.9 (-13.9-70.3)**
Three	330/1095 (30.1%)	605/1584 (38.2%)	**24.4 (10.3-36.2)**
Four	99/175 (56.6%)	158/232 (68.1%)	**33 (-1.6-55.8)**
Age group in years			
<50	285/1107 (25.7%)	559/1625 (34.4%)	**29 (15.3-40.4)**
≥50	158/421 (37.5%)	232/494 (47.0%)	**27.8 (5.4-45.0)**
Underlying health conditions[5]			
No	111/353 (31.4%)	218/505 (43.2%)	**33.5 (10.9-50.3)**
Yes	332/1175 (28.3%)	573/1614 (35.5%)	**23.5 (9.5-35.4)**

[3] Case-participants had symptomatic SARS-CoV-2 infection confirmed by antigen or nucleic acid amplification test; control-participants had a negative SARS-CoV-2 nucleic acid amplification test, with or without symptoms. Vaccination status was assigned on the test date as being eligible to have received a bivalent dose, if ≥67 days after the last monovalent mRNA dose, and as receiving a bivalent dose if ≥7 days after a bivalent mRNA dose and no additional doses were received. Analyses are restricted to participants with complete covariate information.

[4] Vaccine effectiveness calculated using conditional logistic regression, accounting for clustering by four-week enrollment period and U.S. census region. Models comparing VE by subgroup included an interaction term.

[5] Underlying conditions defined using categories defined in Supplementary Table 2

Supplementary Table 7: Supportive analyses for Estimated Effectiveness of a Bivalent mRNA Dose against COVID-19 among U.S. healthcare personnel

Characteristic	No. case-participants who received a bivalent dose / No. eligible (%)[6]	No. control-participants who received a bivalent dose / No. eligible (%)	Adjusted vaccine effectiveness (95% CI)[7]
Model type			
Unconditional, 4-week period by USC region	443/1528 (29.0%)	791/2119 (37.3%)	**32.5 (18.5-44.0)**
Unconditional, 4-week period by USC region	443/1528 (29.0%)	791/2119 (37.3%)	**34.5 (22.4-44.7)**
Conditional, 2-week strata by site	443/1528 (29.0%)	791/2119 (37.3%)	**33.0 (18.3-45.1)**
Conditional, 4-week strata by USC region	443/1528 (29.0%)	791/2119 (37.3%)	**33.9 (21.6-44.3)**
Sensitivity analyses[8]			
Nucleic acid amplification test results only	257/872 (29.5%)	791/2119 (37.3%)	**34.7 (20-46.7)**
Symptomatic illness only	443/1528 (29.0%)	750/2015 (37.2%)	**33.3 (20.8-43.9)**
Not reported to be immunocompromised	431/1492 (28.9%)	763/2052 (37.2%)	**34.2 (21.8-44.6)**
Subgroup analyses[9]			
Sex			
Male	99/284 (34.9%)	159/340 (46.8%)	**45.4 (22.8-61.3)**
Female	344/1244 (27.7%)	632/1779 (35.5%)	**31.1 (17.8-42.2)**
Race and ethnicity			
White, non-Hispanic	352/1111 (31.7%)	638/1547 (41.2%)	**36.9 (24.4-47.3)**
Other race or ethnicity	91/417 (21.8%)	153/572 (26.7%)	**23.7 (-4.8-44.5)**
Highest educational level			
No professional or doctoral degree	326/1270 (25.7%)	570/1736 (32.8%)	**31.8 (18.5-42.9)**
Professional or doctoral degree	117/258 (45.3%)	221/383 (57.7%)	**42.5 (19.2-59.1)**
Anticipated level of patient contact			
Substantial	169/605 (27.9%)	295/817 (36.1%)	**33.7 (15.1-48.3)**
Minimal, moderate, or unknown	270/902 (29.9%)	483/1280 (37.7%)	**32.4 (17.2-44.7)**
Works at hospital or emergency department			
No	127/465 (27.3%)	232/691 (33.6%)	**30.5 (8.2-47.4)**
Yes	316/1063 (29.7%)	559/1428 (39.1%)	**35.8 (22.5-46.8)**
Reason for testing			
Symptoms	390/1345 (29.0%)	558/1560 (35.8%)	**28.1 (14.0-39.9)**
Other	53/183 (29.0%)	192/455 (42.2%)	**47.3 (21.8-64.4)**
Fever, if symptomatic			
No	236/689 (34.3%)	532/1315 (40.5%)	**27.3 (10-41.3)**
Yes	207/839 (24.7%)	218/700 (31.1%)	**25.6 (5-41.7)**
Known recent prior infection[10]			
No	380/1298 (29.3%)	541/1417 (38.2%)	**35.3 (22.6-45.9)**
Yes	63/230 (27.4%)	250/702 (35.6%)	**29.3 (1.0-49.6)**

Abbreviations: USC, U.S. census region

[6] Case-participants had symptomatic SARS-CoV-2 infection confirmed by antigen or nucleic acid amplification test; control-participants had a negative SARS-CoV-2 nucleic acid amplification test, with or without symptoms. Vaccination status was assigned on the test date as being eligible to have received a bivalent dose, if ≥67 days after the last monovalent mRNA dose, and as receiving a bivalent dose if ≥7 days after a bivalent mRNA dose and no additional doses were received. Analyses are restricted to participants with complete covariate information.

[7] Unless otherwise specified, vaccine effectiveness was calculated using conditional logistic regression, accounting for clustering by four-week enrollment period and U.S. census region. Adjusted estimates included the following covariates: age group, sex, race and ethnicity, highest educational level, known community exposure to SARS-CoV-2, prior infection, days since referent dose (most recent monovalent dose). Unconditional models included additional adjustment for U.S. census region and calendar period.

[8] Models restricted to participants with the data specified.

[9] Models comparing vaccine effectiveness by subgroup included an interaction term.

[10] Prior infection was defined as a self-reported positive SARS-COV-2 nucleic acid amplification test or antigen test result >90 days before test date, during Omicron predominance (after 12/19/2021) and during the 12 months before the test date.

Supplementary Table 8: Estimated Vaccine Effectiveness of a bivalent mRNA dose against symptomatic SARS-CoV-2 infection among U.S. healthcare personnel, if leaving out each site

Site excluded	No. case-participants who received a bivalent dose / No. eligible (%)[11]	No. control-participants who received a bivalent dose / No. eligible (%)	Adjusted vaccine effectiveness (95% CI)[12]
1	443/1528 (29.0%)	791/2116 (37.4%)	**34.3 (22.8-44.1)**
2	424/1481 (28.6%)	744/2026 (36.7%)	**33.4 (21.4-43.5)**
3	423/1491 (28.4%)	779/2085 (37.4%)	**36.0 (24.6-45.7)**
4	436/1498 (29.1%)	783/2096 (37.4%)	**32.9 (21.1-43.0)**
5	437/1515 (28.8%)	782/2096 (37.3%)	**34.1 (22.5-44.0)**
6	376/1251 (30.1%)	583/1454 (40.1%)	**36.3 (23.4-47.0)**
7	437/1514 (28.9%)	789/2110 (37.4%)	**34.7 (23.2-44.5)**
8	438/1521 (28.8%)	782/2101 (37.2%)	**34.7 (23.2-44.5)**
9	415/1484 (28.0%)	717/1974 (36.3%)	**35.4 (23.8-45.3)**
10	391/1442 (27.1%)	756/2070 (36.5%)	**37.8 (26.5-47.4)**
11	384/1348 (28.5%)	706/1902 (37.1%)	**34.6 (22.3-45.0)**
12	430/1496 (28.7%)	754/2028 (37.2%)	**33.4 (21.5-43.5)**
13	442/1509 (29.3%)	791/2111 (37.5%)	**33.5 (21.8-43.4)**
14	440/1501 (29.3%)	788/2108 (37.4%)	**32.5 (20.6-42.6)**
15	436/1498 (29.1%)	789/2104 (37.5%)	**33.7 (22.0-43.7)**
16	431/1492 (28.9%)	784/2104 (37.3%)	**35.0 (23.6-44.8)**
17	434/1478 (29.4%)	758/1997 (38.0%)	**34.1 (22.3-44.1)**
18	442/1525 (29.0%)	791/2119 (37.3%)	**34.1 (22.5-43.9)**
19	430/1457 (29.5%)	758/1997 (38.0%)	**35.3 (23.6-45.3)**
20	416/1475 (28.2%)	706/1960 (36.0%)	**33.4 (21.2-43.7)**
21	426/1394 (30.6%)	765/1959 (39.1%)	**32.8 (20.5-43.1)**
22	396/1255 (31.6%)	783/2092 (37.4%)	**31.9 (19.3-42.5)**
23	439/1504 (29.2%)	786/2106 (37.3%)	**33.7 (22.0-43.6)**
24	431/1501 (28.7%)	760/2069 (36.7%)	**32.4 (20.4-42.5)**
25	442/1523 (29.0%)	789/2115 (37.3%)	**34.1 (22.6-44.0)**
26	437/1520 (28.8%)	761/2077 (36.6%)	**32.6 (20.7-42.7)**

[11] Case-participants had symptomatic SARS-CoV-2 infection confirmed by antigen or nucleic acid amplification test; control-participants had a negative SARS-CoV-2 nucleic acid amplification test, with or without symptoms. Vaccination status was assigned on the test date as being eligible to have received a bivalent dose, if ≥67 days after the last monovalent mRNA dose, and as receiving a bivalent dose if ≥7 days after a bivalent mRNA dose and no additional doses were received. Analyses are restricted to participants with complete covariate information.

[12] Vaccine effectiveness was calculated using conditional logistic regression, accounting for clustering by four-week enrollment period and U.S. census region. Adjusted estimates included additional covariates: age group, sex, race and ethnicity, highest educational level, known community exposure to SARS-CoV-2, prior infection, days since referent dose (most recent monovalent dose).

Supplementary Table 9: Relative vaccine effectiveness of receiving three or four monovalent doses, compared with receiving fewer doses, among U.S. healthcare personnel

Vaccination status	Days since last dose (interquartile range)	No. case-participants with specified vaccination status / Total (%)[13]	No. control-participants with specified vaccination status / Total (%)	Adjusted vaccine effectiveness (95% CI)[14]
Monovalent dose 3 compared with monovalent dose 2				
≥67 days after dose 2	581 (451, 671)	244/1009 (24.2%)	275/1254 (21.9%)	**Ref.**
≥67 days after dose 3 [15]	381 (328,436)	765/1009 (75.8%)	979/1254 (78.1%)	**23.3 (2.4-39.7)**
67–359 days after dose 3	315 (280,338)	341/585 (58.3%)	346/621 (55.7%)	**25.2 (-0.1-44.1)**
≥360 days after dose 3	422 (391,463)	424/668 (63.5%)	633/908 (69.7%)	**24.2 (-0.5-42.8)**
Monovalent dose 4 compared with monovalent dose 3				
≥67 days after dose 3	381 (328,436)	765/841 (91.0%)	979/1073 (93.0%)	**Ref.**
≥67 days after dose 4 [16]	171.5 (144,231)	76/841 (9.0%)	74/1053 (7.0%)	**10.3 (-32.3-39.2)**
67–359 days after dose 4	169 (143,227)	74/839 (8.8%)	71/1050 (6.8%)	**10.0 (-33.2-39.2)**
≥360 days after dose 4	398 (390,479)	2/767 (0.3%)	3/982 (0.3%)	[17]

[13] Case-participants had symptomatic SARS-CoV-2 infection confirmed by antigen or nucleic acid amplification test; control-participants had a negative SARS-CoV-2 nucleic acid amplification test, with or without symptoms. Vaccination status was assigned on the test date as being eligible to have received a bivalent dose, if ≥67 days after the last monovalent mRNA dose, and as receiving a bivalent dose if ≥7 days after a bivalent mRNA dose and no additional doses were received. Analyses are restricted to participants with complete covariate information.

[14] Vaccine effectiveness calculated using conditional logistic regression, accounting for clustering by four-week enrollment period and U.S. census region. Adjusted estimates included additional covariates: age group, sex, race and ethnicity, highest educational level, known community exposure to SARS-CoV-2, prior infection, days since referent dose (most recent monovalent dose).

[15] Among participants who were ≥67 days after a monovalent dose 3, the median time since monovalent dose 2 was 671 days (interquartile range, 615, 727).

[16] Among participants who were ≥67 days after a monovalent dose 4, the median time since monovalent dose 3 was 402.5 days (interquartile range, 353, 456).

[17] VE estimate not presented because of sparse data (95% confidence interval >100%)

Supplementary Table 10: Collaborators and other team members acknowledged by site

Site or other affiliation	Study team members acknowledged
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